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Docket No. 49632(71699)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Pamela L. Zeitlin
Serial No.:	09/523,776
Filed:	March 11, 2000
For:	MODULATION OF PROTEIN EXPRESSION USING CARBOCYCLIC ARYL ALKENOIC ACID DERIVATIVES
Examiner:	Shengjun Wang
Art Unit:	1617

Mail Stop: Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION UNDER 37 C.F.R. 1.132

I, Pamela L. Zeitlin, M.D., a citizen of the United States of America residing at 1808 South Road, Baltimore, Maryland 21209, hereby declare as follows:

1. I am a co-inventor of the subject matter described and claimed in the patent application U.S.S.N. 09/523,776, filed on March 11, 2000 and otherwise identified above.

2. I have read and understood the Office Action dated December 27, 2007 and the references cited in the Office Action in the above case.

3. I have previously submitted a declaration dated March 5, 2007 (the "March 5

Declaration") in the above-identified application.

4. In my March 5 Declaration, I described experiments conducted by me or under my supervision relating to certain chemical compounds and their effect on ΔF508-CFTR protein expression in model cells of cystic fibrosis.

5. In my March 5 Declaration, I also stated that the aforementioned results indicate that trans-SAA is surprisingly effective in promoting the trafficking of functional ΔF508-CFTR to the cell surface relative to cinnamic acid and 4-PBA. I further stated that based on that indication that it is my expert opinion that trans-SAA has unexpectedly superior activity relative to cited art compounds cinnamic acid and 4-PBA.

6. I am a co-author of numerous scientific publications relating to the study of cystic fibrosis ("CF"), including "A Pilot Clinical Trial of Oral Sodium 4-Phenylbutyrate (Buphenyl) in ΔF508-Homozygous Cystic Fibrosis Patients", *Am. J. Respir. Crit. Care Med.*, vol. 157, pp. 484-490 (1998) ("Reference A"); and "In Vitro Pharmacologic Restoration of CFTR-mediated Chloride Transport with Sodium 4-Phenylbutyrate in Cystic Fibrosis Epithelial Cells Containing ΔF508-CFTR", *J. Clin. Invest.*, vol. 100(10), pp. 2457-2465 (1997) ("Reference B").

7. In Reference A, first paragraph, the etiology of CF is summarized. In Reference A, first paragraph, it is stated that about seventy (70) % of CF patients carry at least one copy of the most common mutation, the deletion of a phenylalanine residue at position 508 (ΔF508-CFTR), and it is further described that the development of CF results from the functional absence of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) on the cell surface. Thus, promotion of ΔF508-CFTR trafficking is relevant to restoration of CFTR chloride channel function, which addresses the functional absence of CFTR that causes CF.

8. In Reference B, page 2464, first full paragraph, it is stated that "[m]anipulation of aberrant intracellular ΔF508-CFTR trafficking has great promise as a pharmacological treatment for the majority of CF patients."

9. As indicated above in Reference A and Reference B, it is both known in the field and

my expert opinion that about seventy (70) % of CF patients carry at least one copy of the most common mutation, the deletion of a phenylalanine residue at position 508 (ΔF508-CFTR), and as such, trafficking of functional ΔF508-CFTR to the cell surface is a significant, if not primary, mechanism in CF etiology, and thus for a majority of CF patients control of such trafficking is a relevant treatment protocol. On that basis, the declaration in my March 5 Declaration that trans-SAA has unexpectedly superior activity relative to cited art compounds cinnamic acid and 4-PBA in regard to promoting the trafficking of functional ΔF508-CFTR also bears on its unexpectedly superior activity as a CF therapeutic.

10. I, the undersigned Pamela L. Zeitlin, M.D., further declare that all statements made herein of my own knowledge are true and that all statements made upon information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under Section 101 of Title 18 of the United States Code and that such willful false statement may jeopardize the validity of the above identified application or any patent issuing thereon.

By: Pamela L Zeitlin MD

Pamela L. Zeitlin, M.D.

Date: 5/30/08